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SYNCILLIN

Potassium alpha-phenoxyethyl penicillin (Syncillin-Bristol) is not a completely synthesized preparation, as the trade name and the promotion material for this new penicillin suggests. Syncillin is prepared by the synthetic addition of a chemical chain to the penicillin skeleton produced by the usual fermentation process. The chemical change gives the new preparation marked stability in gastric acid; therefore oral administration as a rule produces higher blood levels than equivalent doses of penicillin G.

The manufacturer claims that Syncillin also produces higher blood levels than penicillin V (phenoxymethyl penicillin). Data presented by makers of the latter preparation, which is also resistant to acid degradation, show blood levels as high or higher than those reported with equivalent doses of Syncillin. At this point, it seems reasonable to accept Syncillin as equal to penicillin V and superior to penicillin G in resistance to acid degradation. No other significant advantage for the new preparation has yet been established.

DOSAGE AND BLOOD LEVELS - Following oral administration of Syncillin, peak levels of approximately 2.5 to 5 mcg. per cc. are reached within one-half to one hour after a single 250-mg. dose on an empty stomach. When it is administered with or shortly after meals, significantly lower levels are observed. Measurable blood levels persist for four hours after a single dose; with this product as with penicillin V and other oral penicillins, however, the levels from the second to the fourth hour are significantly lower than those observed after the injection of crystalline or procaine penicillin.

The suggestion that this product makes injectable penicillins unnecessary must be viewed with caution. To maintain the continuous high blood levels required for more severe infections, it would be necessary to administer the antibiotic every four hours around the clock. The manufacturer suggests three-times-a-day dosage of 125 to 250 mg., with larger doses where needed. Increasing the dosage gives higher blood levels as claimed, but in severe infections it cannot be counted on to extend the duration of effective antibacterial levels sufficiently to permit the substitution of Syncillin for a parenteral penicillin.

ANTIBACTERIAL ACTIVITY - Like other penicillins, Syncillin appears in the pleural and ascitic fluids, but it does not cross the blood-brain barrier or ap-

pear in the spinal fluid. The antibacterial spectrum of Syncillin is essentially that of penicillin V and penicillin G. The data presented by the manufacturer indicate that its antibacterial activity on a weight basis is about equal to that of penicillin V, but less than that of penicillin G; therefore no greater antibiotic effect against sensitive organisms can be expected. Although Syncillin is claimed to be effective against more strains of Staphylococcus aureus than the other penicillins, evidence to support this claim is inadequate. Successful treatment with Syncillin of infections caused by staphylococcal organisms resistant to other penicillins has not yet been reported.

Clinical experience thus far has been much too limited to permit evaluation of the allergic potential of Syncillin. There appears to be no reason on theoretical or any other grounds to expect a lower incidence of allergic reactions with Syncillin than with the other oral penicillins.

LIMITATIONS - Neither Syncillin nor any other oral penicillin should be used in the treatment of deep-seated, serious or chronic infections such as endocarditis, meningitis and syphilis. The parenteral administration of penicillin is demanded for such infections, assuming the organisms are sensitive to penicillin. In general, oral penicillins should be used only for treatment of the less severe bacterial infections such as streptococcal pharyngitis and gonococcal urethritis.

Although penicillin is still one of the most useful antibiotics, it has three serious deficiencies: its limited spectrum; the large proportion of bacterial strains, particularly staphylococci, that have become resistant to its action; and an allergic potential which has resulted in many serious reactions. It has not yet been shown that any of these deficiencies will be corrected by Syncillin.

In a comparison of penicillin V with penicillin G in The Medical Letter for July 10, 1959, it was pointed out that with the latter preparation acid degradation is minimized if it is taken on an empty stomach; while penicillin V gives higher blood levels than G, the differences have not been shown to have much clinical significance. Probably the same thing will be true for Syncillin. In general, it has not been demonstrated that one form of oral penicillin is significantly superior to another in antibacterial effectiveness against sensitive strains of staphylococci, streptococci, and gonococci. This point is emphasized because Syncillin, like penicillin V, is much more expensive than penicillin G, and for most patients the high cost must be weighed against the slight advantage of greater resistance to acid degradation.

INFECTIOUS HEPATITIS AND IMMUNE GLOBULIN

Infectious hepatitis (virus A hepatitis, as distinguished from virus B homologous serum hepatitis) occurs the year round, but it generally reaches a peak in the months of January through March. The Communicable Disease Center of the U. S. Public Health Service expects the incidence of the disease to be higher in the winter months of 1960 through 1962 than in previous years, probably reaching epidemic levels in some communities. As this is written, an unusually heavy incidence has been noted on the West Coast and in the Northeast.

The lack of a susceptible laboratory animal and of specific diagnostic serologic tests have handicapped the solution of many problems in prevention, diagnosis and epidemiology of the disease. The virus is present in the blood and the feces; there is conclusive evidence of a fecal-oral route of transmission, but not of a respiratory route. Person-to-person transmission resulting from close contact is considered the most likely mode of spread, but some outbreaks are waterborne, milk-borne, or spread by contaminated food. The infection tends to spread rapidly among school children, who then convey it to adults at home.

More cases occur without jaundice than with it, and such cases are often diagnosed as "intestinal flu." The possibility of infectious hepatitis should be considered when suggestive symptoms occur in any patient with known exposure to hepatitis, or in patients with liver tenderness or enlargement. Positive flocculation tests or increased transaminase levels will help confirm the diagnosis.

USE OF GAMMA GLOBULIN - Immune (gamma) globulin is usually an effective preventive, and should be administered to persons who have had close contact with a patient, even one with a mild infection. Such persons should be made to understand that the virus responsible for a mild, brief attack in one person can cause severe and prolonged disease in another. Since children generally get a much milder form of infectious hepatitis than adults, and since one attack may confer lifelong immunity, some authorities believe that adults should have preference in the use of immune globulin. When it is administered to children, a dose of 0.01 cc. per pound of body weight should provide adequate protection while permitting a modified infection to occur. For adults, a dose of at least 0.02 cc. per pound should be used. Immunity lasts about four to six weeks.

Immune globulin is made by many manufacturers, and may be purchased at a cost to the physician of about $5 for a 2-cc. vial ($6 to $8 to the patient), or about $23 for a 10-cc. vial ($25 to $35 to the patient). Many city and state health departments provide immune globulin for prevention of infectious hepatitis without charge to physicians who request it. In some areas physicians may obtain immune globulin from the Regional Blood Program of the American Red Cross. ("Viral Hepatitis - Clinical and Public Health Aspects" is a comprehensive and practical review prepared by Dr. H. F. Eichenwald of the Cornell Medical School and Dr. J. W. Mosley of the Hepatitis Investigations Unit of the Communicable Disease Center, U. S. Public Health Service. A revised 1959 edition is available for 20¢ from the Superintendent of Documents, Washington 25, D. C.)

ANTI-EPILEPSY DRUGS

The expert use of anticonvulsants has made complete control of seizures possible in roughly 50 per cent of all epileptics, and it has greatly reduced both the frequency and the severity of attacks in another 35 per cent. No single known anticonvulsant drug is equally effective "across the board" in all types of epilepsy. The hydantoins and the barbiturates, for example, are used successfully in the treatment of grand mal, but are generally ineffective against petit mal. The oxazolidinediones are very useful in petit mal, but are essentially useless against grand mal. Hence, accurate diagnosis of seizure-type is necessary.

Once a particular agent is decided on, it should be administered in gradually increasing doses - "titrated" against the frequency of seizures - until either full suppression of seizures is achieved or side effects appear. If side effects, such as drowsiness, ataxia, or blurred vision become troublesome before seizure-control is effected, it may be necessary to lower the dose and add another agent from the same family of drugs. If two or more seizure-types coexist in the same patient, it is necessary to treat each entity separately.

GRAND MAL - In grand mal, diphenylhydantoin U.S.P. (Dilantin--Parke-Davis) is generally the drug of choice, though in infants and some adults phenobarbital is preferred. If Dilantin causes side effects before seizure-control, a barbiturate, preferably phenobarbital, can be added. Contrary to a recent report ("Pulmonary Changes in Hydantoin Therapy," M. T. Moore, JAMA, 171: 1328, 1959) Medical Letter consultants do not believe there is a significant risk of pulmonary changes as a side effect of hydantoin therapy. Mephobarbital U.S.P. (Mebaral-Winthrop) and metharbital (Gemonil-Abbott) are like phenobarbital and offer no distinct advantages to offset their higher cost except that in an occasional patient they may be slightly better tolerated. Primidone U.S.P. (Mysoline-Ayerst) closely resembles phenobarbital in its structure, but is given in larger doses. In small doses it is also a good adjuvant to Dilantin; in larger therapeutic doses it often produces rather pronounced side effects. When Dilantin is poorly tolerated, methylphenylethylhydantoin (Mesantoin-Sandoz) and ethotoin (Peganone-Abbott) are hydantoins which can occasionally be substituted. In general they offer no distinct advantages. Mesantoin has good anticonvulsant properties but occasionally causes agranulocytosis, pancytopenia, and aplastic anemia. Peganone is distinctly less effective as an anticonvulsant than Dilantin.

PETIT MAL - In petit mal two groups of drugs, the oxazolidinediones and the succinamides, are available. The drug of choice is trimethadione U.S.P. (Tridione-Abbott). A newer drug, paramethadione (Paradione-Abbott), which closely resembles it, is neither more potent nor less toxic. Both agents can cause blood dyscrasias and occasionally renal damage. Patients receiving either of these drugs should have frequent blood counts and urinalyses. Among the succinamide derivatives are phensuximide (Milontin--Parke-Davis) and methsuximide (Celontin--Parke-Davis). Both are less effective than the oxazolidinediones, but they may prove useful when the latter are poorly tolerated.

PSYCHOMOTOR SEIZURES - Psychomotor seizures are often very difficult to treat successfully. As a rule, the drugs employed in grand mal are also used in treating psychomotor epilepsy. Mysoline is believed to have some advantage in this condition. Phenacemide (Phenurone-Abbott), a derivative of phenylacetylurea, has also been recommended but it is so toxic that it is rarely employed.

While various combinations of anticonvulsant drugs are available, their use is generally unwise, since the physician must usually tailor an anticonvulsant formula to the needs of the individual patient. Apart from the 15 per cent "hard core" of resistant cases, when drugs fail it is likely to be from erroneous classification of seizure-type, from improper drug choice, from inadequate dosage, from failure of the patient to take medication regularly, from failure to use drugs in combination, from premature withdrawal of drugs, or from unwise lowering of dosage.

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